

FORMULATIONS FOR CONTROLLING HUMAN LICE

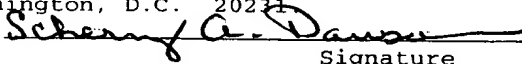
CROSS REFERENCE

5 This application claims priority of Provisional
Application Serial No. 60/091,658 filed July 2, 1998.

Background of the Invention

10 Infestation of the human body by lice is an
increasingly prevalent social and health problem in many
countries, including the United States. Lice are very small
insects (about 2-3mm in length). They deposit eggs either
on a hair or fabric fiber and attach them firmly with a
cementlike excretion. The eggs generally hatch in about six
to ten days, depending on temperature. The empty shells
remaining after the nymphs emerge from the eggs look like
white grains of sand. These shells are called nits.

20 The Anoplura, or sucking lice, are parasites found
on nearly all groups of mammals. Of the 15 recognized
families of Anoplura, two families, *Pediculidae* and
Pthiridae, have species found on humans. *Pediculus humanus*
25 is the only species in the family *Pediculidae* that infests
humans. It includes the head louse, *Pediculus humanus*

"Express Mail" mailing label number	EL342551991US
Date of Deposit	4/5/00
I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 C.F.R. 1.10 on the date indicated above and is addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231	
Scherry A. Dawson	
Printed Name	Signature

2

capitis; and the body or clothing louse, *Pediculus humanus*
humanus, sometimes called *Pediculus corporis*. The crab
louse, *Pthirus pubis*, is a distinct species and is the only
member of the family *Pthiridae* that infests humans. As used
5 herein, the term "human lice or louse" includes a member of
Pediculus humanus or *Pthirus pubis*.

Human lice are spread by crowding and common usage
of clothing and combs. Initially, infestations result at
10 most in irritation, but the irritation can lead to infection
of the irritated area. There are at least three major
diseases that are primarily transmitted by lice: epidemic
typhus, trench fever and relapsing fever.

15 Although the human lice varieties are related,
each of them has specific characteristics with regard to
habitat and feeding. For example, head lice are small hard-
shelled ectoparasites which cling to hair shafts while
feeding, mating and laying eggs. The louse must remain on
20 the head or it will die within a short period of time. Head
lice proliferate at an incredible rate. A louse is ready to
mate and reproduce within 10 hours after hatching. Under
ideal conditions, a female louse may produce up to 300 eggs
in its lifetime. Ideal conditions include an adequate food
25 supply, environmental temperatures from about 28°C. to about
32° C., and relative humidity of about 70% to about 90%.

Poor hygienic and grooming habits are also known to contribute significantly to the spread of lice. Thus, lice infestations are most serious in geographical areas where the inhabitants have both substandard hygienic facilities and practices. Lice can be a problem, however, even when conditions are relatively sanitary.

The louse's hard chitinous exoskeleton serves as protection from external elements. Lice eggs (or ova) are similarly protected by a chitinous sheath surrounding the eggs and attached to the hair shaft. Although lice may be affected by the use of an insecticide, the eggs often remain resistant to attack. Thus, optimum treatment of a lice infestation includes both a pediculicide, which kills the adult lice, and an ovicide, which interrupts the development of the eggs.

Biologically active agents have been used for some time in attempts to control lice. For example, lindane (gamma-benzene hexachloride), organophosphates (malathion), natural pyrethrins, and synthetic compounds known as pyrethroids (such as permethrin) have been used as pediculicides in lice treatment formulations. These agents however, have drawbacks. For example, lindane has a poor safety profile, and lice have developed resistance to it. Natural pyrethrin requires frequent follow-up treatments.

because it provides only short term residual action. Synthetic pyrethroids, although more effective against lice than natural pediculicides, are often more toxic to the subject being treated.

5

Spinosyns (also known as A83453 factors) are agricultural insecticides that have shown activity against 1) southern armyworm and other insects in the order *Lepidoptera*, 2) cotton aphid and other members of the order *Homoptera*, and 3) stable flies, blow flies and mosquitos, which are members of the insect order *Diptera*. (See U.S. Patent No. 5,362,634, infra). Spinosyn A has an excellent human and animal safety and toxicological profile.

10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

This invention provides formulations for controlling infestations of lice in a human comprising a spinosyn, or a physiologically acceptable derivative or salt thereof, and a physiologically acceptable carrier. It also provides methods of using these formulations to control human lice species. These formulations and methods control lice in a safer, more effective manner than previously known anti-lice formulations and methods.

Summary of the Invention

This invention relates to formulations for controlling a lice infestation in a human comprising a

5

spinosyn, or a physiologically acceptable derivative or salt thereof, and a physiologically acceptable carrier. The invention further relates to methods of controlling a lice infestation in a human comprising topically administering to the human an amount of a spinosyn, or a physiologically acceptable derivative/salt thereof, that controls the lice. The formulations and methods of this invention are safer and more effective than those presently available. A particular benefit of these formulations is their effectiveness against louse species that have become resistant to currently used products. Preferred formulations and methods of this invention are hair care formulations, such as shampoos, lotions and conditioners, and methods of using these hair care formulations for controlling a lice infestation in a human.

Detailed Description of the Invention

This invention provides pediculicidal/ovicidal (anti-lice) formulations for controlling a lice infestation in a human comprising as an active ingredient a spinosyn, or a physiologically acceptable derivative or salt thereof, and a physiologically acceptable carrier. Especially useful formulations of this invention are hair-care formulations. Especially useful hair-care formulations are shampoos.

6

5 This invention also provides methods for
controlling a lice infestation in a human comprising
topically administering a formulation comprising a spinosyn
or a physiologically acceptable derivative or salt thereof,
and a physiologically acceptable carrier. In another aspect
this invention provides the use of a spinosyn, or a
physiologically acceptable derivative or salt thereof, or a
formulation containing either an spinosyn or derivative or
salt thereof, for the manufacture of a medicament for
controlling lice in a human.

10 The term "controlling a lice infestation" refers
to treating an active lice infestation or preventing an
infestation in a human who is likely to be exposed to a lice
infestation.

15 Spinosyns are naturally derived fermentation
products. They are macrolides produced by cultivation of
Saccharopolyspora spinosa. The fermentation produces
multifactors, including spinosyn A and spinosyn D (also
20 called A83543A and A83543D). Spinosyn A and spinosyn D are
the two spinosyns that are most active as insecticides. A
product comprised mainly of these two spinosyns
(approximately 85% A and 15% D) is available commercially
25 from Dow Agrosiences under the name spinosad. The name

7

"spinosad" comes from a contraction of the spinosyns "A" and "D".

Each spinosyn has a 12-membered macrocyclic ring that is part of an unusual tetracyclic ring system to which two different sugars are attached, the amino-sugar forosamine and the neutral sugar 2N,3N,4N-tri-O-methylrhamnose. This unique structure sets the spinosyns apart from other macrocyclic compounds.

Spinosyn A (A83543A) was the first spinosyn isolated and identified from the fermentation broth of *Saccharopolyspora spinosa*. Subsequent examination of the fermentation broth revealed that the parent strain of *S. spinosa* produced a number of spinosyns that have been labeled A to J (A83543A to J). Compared to spinosyn A, spinosyns B-J are characterized by differences in the substitution patterns on the amino group of the forosamine, at selected sites on the tetracyclic ring system and on 2N,3N,4N-tri-O-methylrhamnose. The strains of *S. spinosa* currently in use produce a mixture of spinosyns of which the primary components are spinosyn A (~85%) and spinosyn D (~15%). Additional spinosyns, lettered from K to W, have been identified from mutant strains of *S. spinosa*.

8

5 The term "spinosyn or a derivative thereof" as used herein refers to an individual spinosyn factor (A, B, C, D, E, F, G, H, J, K, L, M, N, O, P, Q, R, S, T, U, V, W or Y), an N-demethyl derivative of an individual spinosyn factor, or a combination thereof. For convenience, the term "spinosyn component" will also be used herein to mean an individual spinosyn, or a physiologically acceptable derivative or salt thereof, or a combination thereof.

10 Boeck et al. described spinosyns A-H and J (which they called A83543 factors A, B, C, D, E, F, G, H and J), and salts thereof, in U.S. Patent Nos. 5,362,634 (issued Nov. 8, 1994); 5,496,932 (issued March 5, 1996); and 5,571,901 (issued Nov. 5, 1996). Mynderse et al. described spinosyns L-N (which they called A83543 factors L, M and N), their N-demethyl derivatives, and salts thereof, in U.S. Patent No. 5,202,242 (issued Apr. 13, 1993); and Turner et al. described spinosyns Q-T (which they called A83543 factors Q, R, S and T), their N-demethyl derivatives, and salts thereof, in U.S. Patent Nos. 5,591,606 (issued January 7, 1997) and 5,631,155 (issued May 29, 1997). These patents are incorporated herein by reference. Spinosyns K, O, P, U, V, W and Y are described, for example, by Carl V. DeAmicis, James E. Dripps, Chris J. Hatton and Laura I. Karr in American Chemical Society's Symposium Series: Phytochemicals for Pest Control, Chapter 11, "Physical and

20

25

Biological Properties of Spinosyns: Novel Macrolide Pest-Control Agents from Fermentation", pages 146-154 (1997).

5 The spinosyns can react to form salts. Salts that are physiologically acceptable are also useful in the formulations and methods of this invention. The salts are prepared using standard procedures for salt preparation. For example, spinosyn A can be neutralized with an appropriate acid to form an acid additional salt. The acid addition salts of spinosyns are particularly useful. Representative suitable acid addition salts include salts formed by reaction with either an organic or inorganic acid such as, for example, sulfuric, hydrochloric, phosphoric, acetic, succinic, citric, lactic, maleic, fumaric, cholic, pamoic, mucic, glutamic, camphoric, glutaric, glycolic, phthalic, tartaric, formic, lauric, stearic, salicylic, methanesulfonic, benzenesulfonic, sorbic, picric, benzoic, cinnamic and like acids.

20 In addition to the spinosyn component, the formulations of this invention may further include one or more other compounds that have activity against lice such as, for example, synthetic pyrethroids, natural pyrethrins, and lindane. All ratios, percentages, and parts discussed
25 herein are "by weight" unless otherwise specified.

19

Pediculicidal/Ovicidal Formulations

5 The anti-lice formulations of this invention may be formulated in a number of ways. Particularly useful formulations are shampoos, conditioners, and lotions. These formulations optionally also comprise one or more of the following: a) a surfactant; b) from about 1% to about 10% of a non-volatile silicone material; and/or c) from about 0.5% to about 5% of a suspending agent.

I. Shampoos

10 The shampoo formulations of this invention comprise a spinosyn, or a physiologically acceptable derivative or salt thereof, together with water, a surfactant, and an amide and may optionally comprise another anti-lice agent, a silicone compound, a suspending agent and other cosmetically acceptable components.

15 Human hair becomes soiled due to contact with the surrounding atmosphere and the build up of sebum secreted by the head. When the hair is soiled, it has a dirty feel and an unattractive appearance. The shampoo formulations of this invention both clean the hair and effectively control a lice infestation.

A. Spinosyn Component

20

11

When used in a shampoo formulation, the spinosyn component is present at a level of from about 0.1% to about 30%, preferably from about 1% to about 10%.

5

B. Surfactants

Surfactants suitable for use in these formulations can be any of a wide variety of synthetic anionic, amphoteric, zwitterionic and non-ionic surfactants. Surfactants are generally present in shampoo formulations at a level of from about 5% to about 30%, preferably from about 15% to about 25%.

15

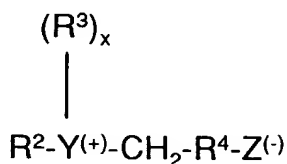
20

25

Examples of synthetic anionic surfactants are the alkali metal salts of organic sulfuric reaction products having an alkyl radical containing from 8-22 carbon atoms and a sulfonic acid or sulfuric acid ester radical (included in the term alkyl is the alkyl portion of higher acyl radicals). Sodium, ammonium, potassium or triethanolamine alkyl sulfates are preferred, especially those obtained by sulfating the higher alcohols (C_8 - C_{18} carbon atoms); sodium coconut oil fatty acid monoglyceride sulfates and sulfonates; sodium or potassium salts of sulfuric acid esters of the reaction product of 1 mole of a higher fatty alcohol (e.g., tallow or coconut oil alcohols) and 1 to 12 moles of ethylene oxide; sodium or potassium salts of alkyl phenol ethylene oxide ether sulfate with 1 to 10 units of

ethylene oxide per molecule and in which the alkyl radicals contain from 8 to 12 carbon atoms; sodium alkyl glyceryl ether sulfonates; the reaction product of fatty acids having from 10 to 22 carbon atoms esterified with isethionic acid and neutralized with sodium hydroxide; and water soluble salts of condensation products of fatty acids with sarcosine.

Examples of zwitterionic surfactants are derivatives of aliphatic quaternary ammonium, phosphonium, and sulfonium compounds, in which the aliphatic radicals can be straight or branched, and wherein one of the aliphatic substituents contains from about 8 to 18 carbon atoms and one contains an anionic water-solubilizing group, e.g., carboxy, sulfonate, sulfate, phosphate, or phosphonate. A general formula for these compounds is:



wherein R^2 contains an alkyl, alkenyl, or hydroxyalkyl radical of from about 8 to about 18 carbon atoms, from 0 to about 10 ethylene oxide moieties and from 0 to 1 glyceryl moiety; Y is a nitrogen, phosphorus, or sulfur atom; R^3 is an alkyl or monohydroxyalkyl group containing 1 to about 3

carbon atoms; x is 1 when Y is sulfur and 2 when Y is nitrogen or phosphorus; R⁴ is alkylene or hydroxyalkylene of from 1 to about 4 carbon atoms, and Z is a carboxylate, sulfonate, sulfate, phosphonate, or phosphate radical.

5

Examples include:

4-[N,N-di(2-hydroxyethyl)-N-octadecylammonio]-butane-1-carboxylate;

5-[S-3-hydroxypropyl-S-hexadecylsulfonio]-3-hydroxy-pentane-1-sulfate;

3-[P,P-diethyl-P-3,6,9-trioxatetradecoxylphosphonio]-2-hydroxypropane-1-phosphate;

3-[N,N-dipropyl-N-3-dodecoxy-2-hydroxypropylammonio]-propane-1-phosphate;

3-(N,N-dimethyl-N-hexadecylammonio)propane-1-sulfonate;

3-(N,N-dimethyl-N-hexadecylammonio)-2-hydroxy-propane-1-sulfonate;

N,N-di(2-hydroxyethyl)-N-(2-hydroxydodecyl) ammonio]-butane-1-carboxylate;

3-[S-ethyl-S-(3-dodecoxy-2-hydroxypropyl)sulfonio]-propane-1-phosphate;

3-[P,P-dimethyl-P-dodecylphosphonio]-propane-1-phosphonate; and

5-(N,N-di(3-hydroxypropyl)-N-hexadecylammonio)-2-hydroxypentane-1-sulfate.

14

Other zwitterionic surfactants, such as betaines, are also useful in the formulations of this invention. Examples of betaines include the higher alkyl betaines, such as coco dimethyl carboxymethyl betaine, lauryl dimethyl carboxymethyl betaine, lauryl dimethyl alpha-carboxyethyl betaine, cetyl dimethyl carboxymethyl betaine, lauryl bis-(2-hydroxyethyl) carboxymethyl betaine, stearyl bis-(2-hydroxypropyl) carboxymethyl betaine, oleyl dimethyl gamma-carboxypropyl betaine and lauryl bis-(2-hydroxypropyl) alpha-carboxyethyl betaine. The sulfobetaines may be represented by coco dimethyl sulfopropylbetaine, stearyl dimethyl sulfopropyl betaine, lauryl dimethyl sulfoethyl betaine, lauryl bis-(2-hydroxyethyl) sulfopropyl betaine, and the like. Amido betaines and amidosulfobetaines, wherein an $RCONH(CH_2)_3$ radical is attached to the nitrogen atom of the betaine, are also useful in the formulations of this invention.

Examples of amphoteric surfactants that can be used in the formulations of this invention are those which are derivatives of aliphatic secondary or tertiary amines in which the aliphatic radical is straight or branched and wherein one of the aliphatic substituents contains from about 8 to about 18 carbon atoms and one contains an anionic water solubilizing group, e.g., carboxy, sulfonate, sulfate, phosphate, or phosphonate. Examples of amphoteric

5 surfactants are sodium 3-dodecylaminopropionate, sodium 3-dodecylaminopropane sulfonate, N-alkyltaurines such as the one prepared by reacting N-dodecylamine with sodium isethionate (see U.S. Pat. 2,658,072, Example 3), N-higher alkyl aspartic acids (see U.S. Pat. 2,438,091), and products sold under the trade name "Miranol" and described in U.S. Pat. 2,528,378.

10 Nonionic surfactants, which are preferably used in combination with an anionic, amphoteric or zwitterionic surfactant, are compounds produced by the condensation of alkylene oxide groups (hydrophilic in nature) with an organic hydrophobic compound, which may be aliphatic or alkyl aromatic in nature. Examples of nonionic surfactants include:

15 1. Polyethylene oxide condensates of alkyl phenols, e.g., the condensation products of alkyl phenols having an alkyl group containing from about 6 to 12 carbon atoms in either a straight or branched chain configuration, with ethylene oxide, the ethylene oxide being present in amounts equal to 10 to 60 moles of ethylene oxide per mole of alkyl phenol. The alkyl substituent in these compounds may be derived from polymerized propylene, diisobutylene, octane, or nonane, for example.

20

25

2. Condensates of ethylene oxide with a product of the reaction of propylene oxide and ethylene diamine products which may be varied in formulation depending upon the desired balance between the hydrophobic and hydrophilic elements. For example, compounds containing from about 40% to about 80% polyoxyethylene by weight and having a molecular weight of from about 5,000 to about 11,000 resulting from the reaction of ethylene oxide groups with a hydrophobic base comprising the reaction product of ethylene diamine and excess propylene oxide, and having a molecular weight on the order of 2,500 to 3,000, are satisfactory.

3. The condensation product of aliphatic alcohols having from 8 to 18 carbon atoms, in either straight or branched chain configuration, with ethylene oxide, e.g., a coconut alcohol ethylene oxide condensate having from 10 to 30 moles of ethylene oxide per mole of coconut alcohol, the coconut alcohol fraction having from 10 to 14 carbon atoms.

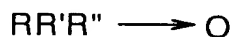
4. Long chain tertiary amine oxides corresponding to the following general formula:

17



wherein R_1 contains an alkyl, alkenyl, or monohydroxy alkyl radical of from about 8 to about 18 carbon atoms, from 0 to about 10 ethylene oxide moieties, and from 0 to 1 glyceryl moiety, and R_2 and R_3 contain from 1 to about 3 carbon atoms and from 0 to about 1 hydroxy group, e.g., methyl, ethyl, propyl, hydroxyethyl, or hydroxypropyl radicals. The arrow in the formula represents a semipolar bond. Examples of amine oxides suitable for use in these formulations include dimethyldodecylamine oxide, oleyldi(2-hydroxyethyl)amine oxide, dimethyloctylamine oxide, dimethyl-decylamine oxide, dimethyl-tetradecylamine oxide, 3,6,9-trioxaheptadecyldiethylamine oxide, di(2-hydroxyethyl)-tetradecylamine oxide, 2-dodecoxyethyldimethylamine oxide, 3-dodecoxy-2-hydroxypropyldi(3-hydroxypropyl) amine oxide, and dimethylhexadecylamine oxide.

5. Long chain tertiary phosphine oxides of the following general formula:



18

wherein R contains an alkyl, alkenyl or monohydroxy-alkyl radical of from about 8 to 18 carbon atoms, from 0 to about 10 ethylene oxide moieties and from 0 to 1 glyceryl moiety, and R' and R'' are each alkyl or monohydroxyalkyl groups containing from 1 to 3 carbon atoms. The arrow in the formula represents a semipolar bond.

Examples of suitable phosphine oxides include: dodecyldimethyl-phosphine oxide, tetradecyldimethylphosphine oxide, tetradecylmethylethylphosphine oxide, 3,6,9-trioxaoctadecyldimethylphosphine oxide, cetyldimethylphosphine oxide, 3-dodecoxy-2-hydroxypropyl-di(2-hydroxyethyl) phosphine oxide, stearyldimethylphosphine oxide, cetylethylpropylphosphine oxide, oleyldiethylphosphine oxide, dodecyldiethylphosphine oxide, tetradecyldiethylphosphine oxide, dodecyldipropylphosphine oxide, dodecyldi(hydroxymethyl)phosphine oxide, dodecyldi(2-hydroxyethyl)phosphine oxide, tetradecylmethyl-2-hydroxypropylphosphine oxide, oleyldimethylphosphine oxide, 2-hydroxydodecyldimethylphosphine oxide.

6. Long chain dialkyl sulfoxides containing one short chain alkyl or hydroxyalkyl radical of 1 to 3 carbon atoms (usually methyl) and one long hydrophobic chain which contains alkyl, alkenyl, hydroxyalkyl, or keto alkyl

radicals containing from about 8 to about 20 carbon atoms, from 0 to about 10 ethylene oxide moieties and from 0 to 1 glyceryl moiety. Examples include: octadecyl methyl sulfoxide, 2-ketotridecyl methyl sulfoxide, 3,6,9-trioxaoctadecyl 2-hydroxyethyl sulfoxide, dodecyl methyl sulfoxide, oleyl 3-hydroxypropyl sulfoxide, tetradecyl methyl sulfoxide, 3-methoxytridecyl methyl sulfoxide, 3-hydroxytridecyl methyl sulfoxide, and 3-hydroxy-4-dodecoxybutyl methyl sulfoxide.

Many additional nonsoap surfactants are described in *McCutcheon's Detergents and Emulsifiers*, 1998 Annual, published by M.C. Publishing Company, Inc.; McCutcheon Division, 175 Rock Rd., Glen Rock, NJ, 07425, U.S.A.

Anionic surfactants, particularly the alkyl sulfates, the ethoxylated alkyl sulfates and mixtures thereof, as well as the amido betaines, are preferred for use in the shampoo formulations of this invention.

C. Amides.

Amides enhance the lathering of the formulations by emulsifying the shampoo components and the active component(s). The amides used in the present formulations can be any of the alkanolamides of fatty acids known for use in shampoos. These are generally mono- and diethanolamides

of fatty acids having from about 8 to about 14 carbon atoms. Other suitable amides are those having multiple ethoxy groups such as PEG-3 lauramide.

5 In the shampoo formulations, the amide is generally present at a level of about 1% to about 7%, preferably from about 2% to about 5%, of the formulation. Preferred amides are coconut monoethanolamide, coconut diethanolamide, and mixtures thereof.

10 **D. Water.**

15 The shampoo formulations of this invention also contain water. Water is typically present in the shampoos at levels of from about 50% to about 80%, preferably from about 60% to about 75%. After adding water, the relative viscosity of the formulation is generally in the range of from about 4,000 centipoise (cp) to about 25,000 cp, preferably from about 4,000 cp to about 12,000 cp, most preferably from about 4,000 cp to about 5,500 cp, measured
20 at 1 RPM at 26.7° for 3 minutes using a Wells-Brookfield viscometer Model DV-CP-2 DVII, Model Cone CP-41. Viscosity modifiers and hydrotropes may be included to bring the formulation's viscosity within these ranges.

E. Optional Components.

1. Silicone compounds may be incorporated into the shampoo formulations to condition the hair and facilitate removal of the dead lice, their eggs and nits. Non-volatile silicone materials are used at levels from about 1% to about 10% of the formulations. Examples of useful silicone compounds are disclosed in U.S. Patent No. 5,292,504, Cardin et al., issued March 8, 1994, incorporated herein by reference.

Non-volatile silicone-containing compounds are preferred and are used at levels of from about 0.1% to about 10%, preferably from about 0.25% to about 3%, by weight of the formulation. Examples of non-volatile silicones are polyalkyl siloxanes, poly alkylaryl siloxanes, polyether siloxane copolymers and mixtures thereof.

Useful polyalkyl siloxanes include, for example, polydimethyl siloxanes (PDMS) with viscosities ranging from about 5 to 15,000,000 cp at 25°. These siloxanes are available, for example, from the General Electric Company as the Viscasil series and from Dow Corning as the Dow Corning 200 series. The viscosity can be measured by means of a glass capillary viscometer as set forth in Dow Corning Corporate Test Method CTM0004, Jul. 20, 1970.

Useful polyalkylaryl siloxanes include polymethylphenyl siloxanes having viscosities of from about 5 to about 15,000,000 cp at 25°. These siloxanes are available, for example, from the General Electric Company as SF 1075 methyl phenyl fluid or from Dow Corning as 556 Cosmetic Grade Fluid.

Useful polyether siloxane copolymers include polypropylene oxide modified polydimethylsiloxanes (available, for example, from Dow Corning as DC-1248), ethylene oxide or mixtures of ethylene oxide and propylene oxide. Water insoluble ones are most useful.

The siloxanes are able to condition the hair due to their ability to lubricate the hair, providing wet and dry combing benefits. Viscous, higher molecular weight siloxanes provide the best conditioning benefits and are, therefore, preferred. Fluids and gums of the siloxane polymers are most desirable. Siloxane polymer gums are rigid as opposed to a liquid or fluid, with high mass molecular weights of from about 200,000 to about 1,000,000 as viscosities from about 100,000 cp to about 150,000,000 cp at 25° C. Such gums are discussed in U.S. Patent No. 5,292,504 (supra).

2. The shampoo formulations may incorporate suspending agents to improve long term stability. Useful suspending agents include fatty amphiphilic crystalline materials having needle-like or platelet structures, polymeric materials, clays, fumed metal oxides, and mixtures thereof. These agents are known in the art (see U.S. Patent No. 5,292,504).

Suitable crystalline amphiphilic materials are those that have needle or platelet-type structures. Such compounds include long chain (C_{16} - C_{22}) acyl derivatives, such as ethylene glycol esters of fatty acids (e.g., ethylene glycol distearate); long chain (C_{16} - C_{22}) alkanol amides of fatty acids, such as stearamide MEA, stearyl stearate, and distearyl dithiopropionate; and mixtures thereof.

Polymeric materials that are useful as suspending agents include cross-linked polyacyclic acids (such as the Carbopol series, available from the B.F. Goodrich Chemical Company), guar gum and its derivatives, xanthan gum, cross linked copolymers of ethylene/maleic anhydrides, and mixtures thereof.

Clays and fumed metal oxides are also effective suspending agents. Examples include magnesium aluminum silicates (such as the Veegum series, available from R. T.

Vanderbilt Company, Inc.), sodium aluminum silicates (such as the Laponite series, available from Laponite United States), fumed silica, fumed alumina, fumed titania and mixtures thereof.

5

In the shampoo formulations of this invention suspending agents are generally present in amounts of from about 0.5% to about 5%, preferably from 0.5% to about 3%. The long chain acyl derivatives such as ethylene glycol esters of fatty acids are preferred. Most preferred is ethylene glycol distearate.

3. The shampoo formulations can also contain a variety of other components suitable for rendering the formulations more cosmetically acceptable. Such optional ingredients are known in the art and include, e.g., preservatives, such as methyl paraben, propyl paraben, methylisothiazolinone and imidazolidinyl urea; thickeners and viscosity modifiers, such as amine oxides, block polymers of ethylene oxide and propylene oxide (such as Pluronic F88 offered by BASF Wyandotte), fatty alcohols (such as cetearyl alcohol), sodium chloride, ammonium chloride, sodium sulfate, polyvinyl alcohol, propylene glycol, and ethyl alcohol; hydrotropes, such as xylene sulfonate; pH adjusting agents, such as citric acid, succinic acid, phosphoric acid, sodium hydroxide, and sodium

carbonate; perfumes, dyes, quaternary ammonium compounds, such as Polyquaternium 41, sequestering agents, such as disodium ethylenediamine tetraacetate; and pearlescing agents, such as distearic acid ester of ethylene glycol, stearic acid and palmitic acid diesters of polyethylene glycol, and stearic acid monoethanolamine. Generally, these optional components are used individually at a level of from about 0.1% to about 10% of the formulation.

The shampoo formulations of this invention are used in a conventional manner for cleaning hair. From about 10 g to about 30 g of a formulation is applied to wet hair and worked through both hair and scalp. The formulation is left on the hair and scalp for approximately 6-10 minutes and then is removed by rinsing. This process is repeated until the hair is clean.

A useful pediculicidal shampoo of this invention comprises:

(a) from about 0.1% to about 2.5% of a spinosyn, or a physiologically acceptable derivative or salt thereof;

(b) from about 5% to about 30% of a synthetic surfactant;

(c) from about 1% to about 7% of an amide; and

(d) water.

II. Hair Conditioner Formulations

5 The hair conditioning formulations of this invention comprise a spinosyn component and a conditioner and may optionally comprise another anti-lice agent, such as permethrin or lindane. These conditioner formulations may also be used effectively to treat a lice infestation.

10 Hair conditioners are products that improve the appearance, feel and manageability of hair. Conditioners are particularly important when the hair has been damaged by treatments such as permanent waving, dyeing, teasing, and bleaching, or by atmospheric conditions, such as sunlight, that cause photo-catalyzed oxidation. These factors may cause hair to have poor texture, making it difficult to manage and comb, whether wet or dry.

15 Conditioning products are well known and include "rinse-type" products , which are rinsed off shortly after being applied to clean hair, and "deep conditioners" which remain on the hair for extended periods of time.

A. Spinosyn Component

When used in hair conditioner formulations, the spinosyn component is present at a level of from about 0.1% to about 30%, preferably from about 1% to about 10%.

5

B. Conditioners

One group of conditioners useful in the hair conditioner formulations of this invention are long chain quaternary ammonium compounds combined with lipid materials, such as fatty alcohols (see U.S. Pat. No. 3,155,591, Hilfer, issued Nov. 3, 1964, and U.S. Pat. No. 4,269,824, Villamarin, et al., issued May 26, 1981). Another group of conditioners are lipids and quaternary ammonium compounds. These conditioners are used to form gel-type conditioner products having good in-use cosmetic and rheological characteristics. These types of gel-type formulations are generally described in the following documents: Barry, "The Self Bodying Action of the Mixed Emulsifer Sodium Docecyl Sulfate/Cetyl Alcohol", *J. of Colloid and Interface Science*, **28**, 82-91 (1968); Barry et al., "The Self-Bodying Action of Alkyltrimethylammonium Bromides/Cetostearyl Alcohol Mixed Emulsifiers; Influence of Quarternary Chain Length", *J. of Colloid and Interface Science*, **35**, 689-708 (1971); and Barry et al., "Rheology of Systems Containing Cetomacrogol/1000 - (cetostearyl alcohol), I. Self-Bodying Action", *J. of Colloid and Interface Science*, **38**, 616-625 (1972).

1554344 "040509"

20

25

1. Lipid Materials. The lipid materials used in these conditioners are present at a level of from about 0.5% to about 3%. These lipids are essentially water-insoluble, and contain hydrophobic and hydrophilic moieties. They include natural and synthetically-derived fatty materials selected from acids, acid derivatives, alcohols, esters, ethers, ketones, amides, and mixtures thereof, having alkyl chain lengths from about 12 to about 22 carbon atoms, preferably from 16 to 18 carbon atoms in length. Fatty alcohols and fatty esters are preferred.

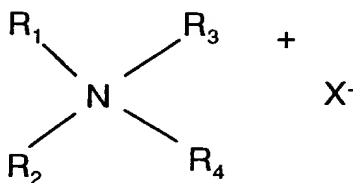
Useful fatty alcohols are known (see, for example, U.S. Pat. No. 3,155,591, supra; U.S. Pat. No. 4,165,369 (Watanabe et al., issued May 26, 1981); British Patent Specification 1,532,585, published Nov. 15, 1978; Fukushima et al., "The Effect of Cetostearyl Alcohol in Cosmetic Emulsions", *Cosmetics & Toiletries*, **98**, 89-102 (1983); and Hunting, *Encyclopedia of Conditioning Rinse Ingredients*, at 204 (1987). Fatty alcohols are C₁₂-C₁₆ alcohols selected from cetearyl alcohol, cetyl alcohol, isostearyl alcohol, lanolin alcohol, lauryl alcohol, oleyl alcohol, stearyl alcohol, and mixtures thereof. Preferred are cetyl alcohol, stearyl alcohol, and mixtures thereof. A particularly preferred fatty alcohol is comprised of a mixture of cetyl alcohol and stearyl alcohol containing from about 55% to about 65% (by weight of mixture) of cetyl alcohol.

Useful fatty esters are also known (see Kaufman, et al., U.S. Pat. No. 3,341,465, issued Sep. 12, 1967). Fatty esters are fatty acids in which the active hydrogen has been replaced by the alkyl group of a monohydric alcohol. The monohydric alcohols are fatty alcohols as described, supra. The fatty esters useful in these conditioner formulations include cetyl lactate, cetyl octanoate, cetyl palmitate, cetyl stearate, glyceryl monostearate, glyceryl laurate, glyceryl myristate, glyceryl oleate, glyceryl stearate, glyceryl monoacetate, and mixtures thereof. Cetyl palmitate and glycerol monostearate, or mixtures thereof, are preferred.

2. Surfactants. Cationic surfactants may be used in these conditioning formulations, either singly or in combination, generally at a level of from about 0.1% to about 5% of the final formulation. These surfactants contain amino or quaternary ammonium hydrophilic moieties that are positively charged when dissolved in the aqueous formulations of this invention. These cationic surfactants are known in the art (see McCutcheon's *Detergents & Emulsifiers*, supra; Schwartz et al., *Surface Active Agents, Their Chemistry and Technology*, New York: Interscience Publishers, 1949; U.S. Pat. No. 3,155,591, supra; U.S. Pat. No. 3,929,678 (Laughlin et al., issued Dec. 30, 1975); U.S.

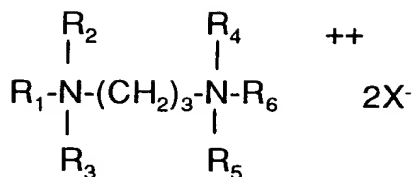
Pat. No. 3,959,461 (Bailey et al., issued May 25, 1976); and
U.S. Pat. No. 4,387,090 (Bolich, Jr., issued Jun. 7, 1983).

Useful quaternary ammonium cationic surfactant
materials are those of the general formula:



wherein R_1 is hydrogen, an aliphatic group of from 1 to 22 carbon atoms, or an aromatic, aryl or alkylaryl group having from 12 to 22 carbon atoms; R_2 is an aliphatic group having from 1 to 22 atoms; R_3 and R_4 are each alkyl groups having from 1 to 3 carbon atoms, and X is an anion selected from halogen, acetate, phosphate, nitrate and alkyl sulfate radicals. The aliphatic groups may contain ether linkages, and other groups such as amido groups, in addition to carbon and hydrogen atoms.

Other useful quaternary ammonium salts have the formula:



wherein at least one, but no more than 3, of the R groups is an aliphatic group having from 16 to 22 carbon atoms, and the remaining R groups are selected from hydrogen and alkyl groups having from 1 to 4 carbon atoms, and X is an ion selected from halogen, acetate, phosphate, nitrate and alkyl sulfate radicals. Tallow propane diammonium dichloride is an example of this type of quaternary ammonium salt.

Quaternary ammonium salts useful herein also include dialkyldimethylammonium chlorides wherein the alkyl groups have from 12 to 22 carbon atoms. These alkyl groups may be derived from long-chain fatty acids, such as hydrogenated tallow fatty acid. Tallow fatty acid gives rise to quaternary compounds wherein R₁ and R₂ predominantly have from 16 to 18 carbon atoms. Examples include ditallow dimethyl ammonium chloride, ditallow dimethyl ammonium methyl sulfate, dihexadecyl dimethyl ammonium chloride, di(hydrogenated tallow) dimethyl ammonium chloride, dioctadecyl dimethyl ammonium chloride, dieicosyl dimethyl ammonium chloride, didocosyl dimethyl ammonium chloride,

di(hydrogenated tallow) dimethyl ammonium acetate,
dihexadecyl dimethyl ammonium chloride, dihexadecyl dimethyl
ammonium acetate, ditallow dipropyl ammonium phosphate,
ditallow dimethyl ammonium nitrate, di(coconutalkyl)
5 dimethyl ammonium chloride, and stearyl dimethyl benzyl
ammonium chloride. Preferred quaternary ammonium salts
useful herein include ditallow dimethyl ammonium chloride,
dicetyl dimethyl ammonium chloride, stearyl dimethyl benzyl
ammonium chloride, cetyl trimethyl ammonium chloride,
10 tricetyl methyl ammonium chloride, and mixtures thereof.
Di(hydrogenated tallow) dimethyl ammonium chloride
(Quaternium-18) is a particularly preferred quaternary
ammonium salt, and is available from the Sherex Chemical
Company, Inc. as Adogen 442 and Adogen 442-100P.

15
20
25
Salts of primary, secondary and tertiary fatty
amines may also be used as a cationic surfactant. The alkyl
groups of such amines preferably have from 12 to 22 carbon
atoms, and may be substituted or unsubstituted. Secondary
and tertiary amines are preferred; and tertiary amines are
particularly preferred. Examples of useful amines include
stearamido propyl dimethyl amine, diethyl amino ethyl
stearamine, dimethyl stearamine, dimethyl soyamine,
soyamine, myristyl amine, tridecyl amine, ethyl
stearylamine, N-tallowpropane diamine, ethoxylated (5 moles
E.O.) stearylamine, dihydroxy ethyl stearylamine, and

arachidylbehenylamine. Suitable amine salts include the halogen, acetate, phosphate, nitrate, citrate, lactate and alkyl sulfate salts. Examples include stearylamine hydrochloride, soyamine chloride, stearylamine formate, N-tallowpropane diamine dichloride and stearamidopropyl dimethylamine citrate. Useful cationic amine surfactants are also disclosed in U.S. Pat. No. 4,275,055 (Nachtigal et al., issued Jun. 23, 1982).

3. Water. Water is an essential ingredient in the conditioner formulations. Water is added as the last step in preparing the conditioner, using an amount sufficient to bring (q.s.) the mixture to 100%.

4. Optional Ingredients. Silicone conditioning agents may be used for their cosmetic and rheological characteristics. Silicone oils and silicone polymers are well known conditioning agents. For example, volatile silicones, organosilicone polymers in water-alcohol mixtures, and volatile silicone fluids are disclosed in U.S. Patent No. 5,292,502, supra.

The formulation may include one or more silicones disclosed for use in the shampoo formulations supra. These silicones include volatile and non-volatile polyalkyl siloxanes, polyalkylaryl siloxanes, and mixtures thereof.

They may be used at levels from about 0.2% to about 5% of the final formulation.

5 As with shampoos, the higher viscosity silicone gums of the siloxanes disclosed supra are preferred. These gums are rigid, as opposed to a fluid, with high molecular weights of from about 200,000 to about 1,000,000 and viscosities from about 100,000 cp to about 150,000,000 cp at 25°. Most preferred are the polydimethylsiloxane gums.

10 Often a significant amount of the lipid material in the conditioner is deposited on the hair, leaving it greasy. The conditioner formulations may, therefore, incorporate silicone copolyols to provide optimum conditioning benefits with the anti-lice treatment. See European Patent Application 155,806, published Sep. 25, 1985.

15 The silicone copolyols are polyalkylene oxide modified dimethylpolysiloxanes, herein referred to as a "dimethicone copolyols" that act as an emulsifier and reduce the deposition of the vehicle materials (lipid materials and/or cationic surfactants) on the hair. Useful dimethicone copolyols are also disclosed in U.S. Patent No. 5,292,504, supra.

The silicone copolyol is generally present at a level of from about 0.1% to about 10%, preferably from about 0.1% to about 2%, of the final formulation.

5 Dimethicone copolyols are preferred for this use. Dow Corning 190 Silicone Surfactant is a preferred dimethicone copolyol.

10 The formulations may also contain components that modify the physical and performance characteristics of the conditioning product. Such components include additional surfactants, salts, buffers, thickeners, solvents, opacifiers, pearlescent aids, preservatives, fragrance, colorants, dyes, pigments, chelators, sunscreens, vitamins, and medicinal agents. Examples of these types of components are disclosed in U.S. Pat. No. 4,387,090 (Bolich, Jr., issued Jun. 7, 1983).

20 The formulations may also contain optional surfactant materials at levels such that the total level of surfactant present in the formulation (including the cationic surfactant vehicle material, described supra) is from about 0.05% to about 5%. These optional surfactant materials may be anionic, nonionic or amphoteric. Examples are cetareth-20, steareth-20, sorbitan monoesters, sodium tallow alkylsulfate, and tallow betaine. Optional

25

surfactant materials are described in McCutcheon's *Detergents & Emulsifiers*, supra; Schwartz et al., supra; and U.S. Pat. No. 3,929,678 supra.

5 Preferred optional surfactant materials are nonionic. Such surfactants are most commonly produced by the condensation of an alkylene oxide (hydrophilic in nature) with an organic hydrophobic compound that is usually aliphatic or alkyl aromatic in nature. The length of the hydrophilic or polyalkylene moiety that is condensed with any particular hydrophobic compound can be adjusted to yield a water-soluble compound having the desired degree of balance between hydrophilic and hydrophobic elements. Such nonionic surfactants include polyethylene oxide condensates of alkyl phenols, condensation products of aliphatic alcohols with ethylene oxide, condensation products of ethylene oxide with a hydrophobic base formed by condensation of propylene oxide with propylene glycol, and condensation products of ethylene oxide with the product resulting from the reaction of propylene oxide and ethylene diamine. Another variety of nonionic surfactant is a non-polar nonionic surfactant, typified by the amine oxide surfactants. Preferred nonionic surfactants include cetareth-20, steareth-20 and ceteth-2.

10
15
20
25

37

Salts and buffers may also be added in order to modify the product rheology. For example, salts such as potassium chloride, ammonium chloride, and sodium chloride, may be added at levels of from about 0.001% to about 1%. Buffers, such as citrate or phosphate buffers, may also be added. The present formulations as finally formulated preferably have a pH of from about 3 to about 10, most preferably from about 3 to about 7.

Additional conditioning components may also be incorporated into the formulations. For example, proteins may be added at levels of from about 0.1% to about 10%. Cationic proteins may also serve as surfactant vehicle materials.

Thickening agents are preferred optional components. Such thickeners include nonionic thickening agents that are incorporated at levels of from about 0.1% to about 8%. Such agents are polymers that exhibit viscosities exceeding about 20,000 cp at low shear (about 10^{-2} sec⁻¹). Examples are polyoxyethylene, guar gum, methylcellulose, methyl hydroxypropyl cellulose, polypropyl cellulose, polypropyl hydroxyethyl cellulose, hydroxyethyl cellulose, starches and starch derivatives, and mixtures thereof. Nonionic thickening agents are disclosed in U.S. Pat. No. 4,387,090 (Bolich et al., issued Jun. 7, 1983).

5 The thickening agents are used to bring the viscosity of the formulation from about 10,625 cp to about 14,375 cp (as measured with a Wells-Brookfield viscometer, Model RVT DV-CP-2, DV-11, Model Cone CP-52, using ¼ mL at 1 rpm at 26.7°. for 1 minute).

10 The hair conditioning formulations of this invention are generally used on the hair after all shampoo has been removed by rinsing with water.

15 This invention also provides a method for treating human hair to kill and facilitate removal of lice and their eggs, comprising the steps of:

- 20 (a) applying from about 10 grams to about 30 grams of a formulation of this invention to the wet hair;
- (b) working the formulation through the hair and scalp;
- (c) leaving the formulation on the hair and scalp for about 6-10 minutes; and
- (d) removing the formulation from the hair by rinsing with water.

III. Lotions

25 Anti-lice lotions comprising a spinosyn, or a physiologically acceptable derivative or salt thereof, and a

lotion carrier are another aspect of this invention. These lotions can be applied directly onto the hair in liquid form or in spray form. They are formulated to be applied to the hair for a period of time and not immediately removed by rinsing with water.

A. Spinosyn Component

When used in a lotion formulation of this invention, the spinosyn component is generally present at a level of from about 0.1% to about 30%, preferably from about 1% to about 10%.

B. Liquid Vehicle

In addition to the spinosyn component, the lotion formulations of this invention comprise a liquid vehicle such as alcohol, water or a mixture thereof, to assist in delivery of the spinosyn component to the hair. Suitable alcohols are monohydric alcohols such as methanol, ethanol, isopropanol, or mixtures thereof. Since alcohols can have a deleterious effect upon the stability of the formulations, water alone is most preferred as the vehicle. The vehicle is added in an amount necessary to q.s. the formulation to 100%.

C. Optional Components

5 The lotion formulations of this invention may include optional components to provide benefits to the hair in addition to the anti-lice activity. Optional components include: preservatives and antimicrobials, such as DMDM hydantoin and tetrasodium EDTA; pH balancing agents, such as sodium citrate and citric acid; emulsifiers, such as PEG-60 castor oil; and thickeners and viscosity modifiers, such as polyvinylpyrrolidone. When included, such components generally are used individually at a level from about 0.01% to about 10%.

15 Conditioning agents may be included to facilitate the removal of dead lice and eggs from the hair and to provide good wet and dry combing. The same types of conditioning agents described in the conditioning formulations supra may be used in the lotions; these include quaternary ammonium salts, fatty amines and mixtures thereof. Conditioning agents are used at levels from about 20 0.1% to about 1%, preferably from about 0.4% to about 0.6%.

25 Preferred conditioning agents are quaternary ammonium salts. Preferred quaternary ammonium salts include dialkyldimethylammonium chlorides, wherein the alkyl groups have from 12 to 22 carbon atoms. These alkyl groups may be derived from long-chain fatty acids, such as hydrogenated

41

5 tallow fatty acid. Tallow fatty acid gives rise to quaternary compounds wherein R_1 and R_2 predominantly have from 16 to 18 carbon atoms. Examples of quaternary ammonium salts useful in the lotion formulations include di(hydrogenated) tallow dimethyl ammonium chloride, dicetyl dimethyl ammonium chloride, tricetyl methyl ammonium chloride, cetyl trimethyl ammonium chloride, stearyl dimethyl benzyl ammonium chloride, and mixtures thereof. Most preferred is dicetyl dimethyl ammonium chloride.

10 Alcohol synergizers may also be added to the lotion formulations to enhance their anti-lice activity. The alcohols used in the lotion formulations are selected from phenyl C_2 - C_6 alkanols, phenyl C_2 - C_6 diols, C_2 - C_8 alkylene diols, and mixtures thereof. These synergizers may be included at levels from about 0.25% to about 10%, wherein the level of phenyl alkanols, phenyl diols, and mixtures thereof, does not exceed 5% of the formulation. Preferably, the level is about 0.5% to about 5% of the formulation, most preferably from about 2% to about 4%. A preferred synergizer is hexylene glycol.

20 The lotion formulations of this invention are applied directly to the hair. The amount of lotion used is generally from about 10 mL to about 50 mL. The lotion is worked through the hair and left on the hair for about 10 minutes, preferably about 30 minutes. The hair is then

42

cleansed, generally with a shampoo, before rinsing with water.

The following examples illustrate the formulations of this invention:

5

Example 1

A lotion formulation is prepared as follows:

<u>Component</u>	<u>Weight (%)</u>
Polyvinylpyrrolidone	0.50
DMDM hydantoin	0.20
Tetrasodium EDTA	0.13
Citric acid	0.05
PEG-60 castor oil	0.50
Hexylene glycol	4.00
Dicetyl dimethyl ammonium chloride	0.38
Spinosyn A	0.50
Water	q.s. to 100.00

Add the spinosyn to a tank containing a mixture of

PEG-60 castor oil, hexylene glycol, propylene glycol and dicetyl dimethyl ammonium chloride at between 35° to 38°.

In a second tank, mix polyvinyl pyrrolidone, DMDM hydantoin, tetrasodium EDTA and citric acid and bring the mixture to a temperature between 35° to 38°. Add the contents of the first tank to the second tank and mix until uniform. Cool the mixture to about 27°, and empty into storage drums.

Example 2

43

A lotion formulation is prepared using the procedure described in Example 1, but with the following formula.

5

10

15

20

25

30

35

40

45

50

55

60

65

70

75

80

85

90

95

100

105

110

115

120

125

130

135

140

145

150

155

160

165

170

175

180

185

190

195

200

205

210

215

220

225

230

235

240

245

250

255

260

265

270

275

280

285

290

295

300

305

310

315

320

325

330

335

340

345

350

355

360

365

370

375

380

385

390

395

400

405

410

415

420

425

430

435

440

445

450

455

460

465

470

475

480

485

490

495

500

505

510

515

520

525

530

535

540

545

550

555

560

565

570

575

580

585

590

595

600

605

610

615

620

625

630

635

640

645

650

655

660

665

670

675

680

685

690

695

700

705

710

715

720

725

730

735

740

745

750

755

760

765

770

775

780

785

790

795

800

805

810

815

820

825

830

835

840

845

850

855

860

865

870

875

880

885

890

895

900

905

910

915

920

925

930

935

940

945

950

955

960

965

970

975

980

985

990

995

1000

<u>Component</u>	<u>Weight (%)</u>
Polyvinylpyrrolidone	0.50
DMDM hydantoin	0.20
Tetrasodium EDTA	0.13
Citric acid	0.05
PEG-60 castor oil	0.50
Hexylene glycol	2.00
Propylene glycol	2.00
Dicetyl dimethyl ammonium chloride	0.38
Spinosad	0.25
Water	q.s. to 100.00

Example 3

A lotion formulation is prepared by the procedure described in Example 1, but with the following formula:

25

30

35

40

45

50

55

60

65

70

75

80

85

90

95

100

105

110

115

120

125

130

135

140

145

150

155

160

165

170

175

180

185

190

195

200

205

210

215

220

225

230

235

240

245

250

255

260

265

270

275

280

285

290

295

300

305

310

315

320

325

330

335

340

345

350

355

360

365

370

375

380

385

390

395

400

405

410

415

420

425

430

435

440

445

450

455

460

465

470

475

480

485

490

495

500

505

510

515

520

525

530

535

540

545

550

555

560

565

570

575

580

585

590

595

600

605

610

615

620

625

630

635

640

645

650

655

660

665

670

675

680

685

690

695

700

705

710

715

720

725

730

735

740

745

750

755

760

765

770

775

780

785

790

795

800

805

810

815

820

825

830

835

840

845

850

855

860

865

870

875

880

885

890

895

900

905

910

915

920

925

930

935

940

945

950

955

960

965

970

975

980

985

990

995

1000

<u>Component</u>	<u>Weight (%)</u>
Polyvinylpyrrolidone	0.50
DMDM hydantoin	0.20
Tetrasodium EDTA	0.13
Citric acid	0.05
Isopropanol	1.00
PEG-60 castor oil	0.50
Hexylene glycol	4.00
Dicetyl dimethyl ammonium chloride	0.60
Spinosyn component	0.10
Water	q.s. to 100.00

To control a lice infestation, the lotion formulations of Examples 1-3 are applied to the hair and

44

left on for at least ½ hour before being removed by shampooing or rinsing.

Example 4

A shampoo formulation is prepared as follows:

<u>Component</u>	<u>Weight (%)</u>
Ammonium laureth sulfate	10.40
Ammonium lauryl sulfate	9.50
Coconut monoethanolamide	4.00
Ethylene glycol distearate	3.00
DMDM hydantoin	0.20
Monosodium phosphate	0.10
Disodium phosphate	0.25
Citric acid	0.07
Ammonium xylenesulfonate	1.58
Spinosyn A	0.50
Water	q.s. to 100.00

Add the ammonium lauryl sulfate to a tank and heat to between about 66° to about 69°. While maintaining this temperature, add an aqueous solution of mono-sodium phosphate and then an aqueous solution of disodium phosphate. Upon reaching 69°, add the ammonium xylenesulfonate to the mixture and heat to from about 74° to 77°; add the coconut monoethanolamide, mixing until well dispersed, the ethylene glycol distearate and about 4.5% of the water. Continue mixing until homogeneous and cool mixture to about 41°. Pump the mixture into a second tank and add the ammonium laureth sulfate, DMDM hydantoin, and aqueous solution of citric acid. Add the a spinosyn to the

second tank and q.s. to 100% with water. Mix thoroughly, cool to about 27°, and pump the mixture into storage drums.

Example 5

5 A shampoo formulation is prepared as follows:

<u>Component</u>	<u>Weight</u>
Ammonium laureth sulfate	14.15
Ammonium lauryl sulfate	3.14
Coconut monoethanolamide	3.00
Ethylene glycol distearate	3.00
Silicone gum ¹	0.50
Dimethicone fluid (350 cp)	0.50
Tricetyl methyl ammonium chloride	0.29
Cetyl alcohol	0.42
Stearyl alcohol	0.18
DMDM hydantoin	0.20
Sodium chloride	0.90
Ammonium chloride	0.05
Ammonium xylenesulfonate	1.25
Spinosad	0.40
Water	q.s. to 100.00

SE-76 Gum.

¹Silicone gum available from The General Electric Co. as SE-30 or

25 Add approximately 0.5% of the ammonium laureth sulfate and the dimethicone to a container, and mix for approximately 30 minutes. Add approximately 2% ammonium laureth sulfate to a processing tank and heat to 68° to 71°.

30 Add about 0.12% stearyl alcohol, about 0.06% of cetyl alcohol, and the contents of the first container to the processing tank. Mix until uniform, maintaining the mixture between 68° and 71°. To a second processing tank, add

46

ammonium lauryl sulfate and heat to about 71°. While maintaining this temperature, add 0.05% ammonium chloride, about 18% water, ammonium xylenesulfonate and the remainder of the stearyl and cetyl alcohols. Add coconut monoethanolamide, tricetyl methyl ammonium chloride, ethylene glycol distearate, approximately half the DMDM hydantoin and the contents of the first tank to the second tank while maintaining a temperature of about 77°. Mix until homogenous and then cool to about 41°. Pump to a third tank and add the remainder of the ammonium laureth sulfate, DMDM hydantoin, and sodium chloride. Add the spinosyn to the mixture and q.s. to 100% with water. Mix thoroughly, cool to about 27°, and pump the mixture into storage drums.

Example 6

A shampoo formulation is prepared as follows:

<u>Component</u>	<u>Weight %</u>
Ammonium laureth sulfate	12.81
Ammonium lauryl sulfate	9.10
Coconut monoethanolamide	2.30
Isostearyl ethylmidonium ethosulfate	1.25
DMDM hydantoin	0.20
Monosodium phosphophate	0.50
Disodium phosphate	0.38
Sodium chloride	0.04
Citric acid	0.10

47

Ammonium xylenesulfonate	1.35
Spinosyn component	0.56
Water	q.s. to 100.00

5 Add about 6.5% of the water and the ammonium laureth sulfate to a mixing tank and heat the mixture to about 35°. While maintaining this temperature, add the following components individually in sequence, mixing so that each component is well mixed into the batch: ammonium lauryl sulfate, ammonium xylenesulfonate, monosodium phosphate, disodium phosphate, DMDM hydantoin, sodium chloride, a solution of citric acid and water, a solution of coconut diethanolamide and isostearyl ethylmidonium ethosulfate. Add the spinosyn to the mixture, and q.s. to 100% with water. Mix thoroughly, cool to about 27°, and pump the mixture into storage drums.

Example 7

20 A conditioner formulation of this invention is prepared as follows:

ST, 0480

<u>Component</u>	<u>Weight %</u>
Cetyl alcohol	1.00
Stearyl alcohol	0.72
DMDM hydantoin	0.20
Hydroxyethyl cellulose	0.50
Quaternium-18	0.85
Ceteareth-20	0.35
Stearalkonium chloride	0.85

48

	Glyceryl monostearate	0.25
	Citric acid	0.08
	Silicone gum ¹	0.30
	Cyclomethicone fluid	1.70
5	Spinosyn A	1.00
	Water	q.s. to 100.00

¹ Silicone gum available from The General Electric Co. as SE-30 or SE-76 Gum.

10 Combine all components, except the DMDM hydantoin, citric acid, silicone gum, cyclomethicone, and a spinosyn, in a processing tank and heat the mixture to about 88°. After the solution is thoroughly mixed, cool it to approximately 48°. In a separate tank, premix the silicone gum and cyclomethicone, with heat and agitation to form a gum solution. Add the spinosyn to this mixture. Add the gum solution and all the remaining components, and q.s. with water. Mix thoroughly, cool to about 27°, and pump the mixture into storage drums.

Example 8

25 A conditioner formulation is prepared by the procedure described in Example 7, but using the following formula:

30 FT, 0490

<u>Component</u>	<u>Weight %</u>
Cetyl alcohol	1.00
Stearyl alcohol	0.72

49

DMDM hydantoin	0.20
Hydroxyethyl cellulose	0.50
Quaternium-18	0.85
Ceteareth-20	0.35
Stearamidopropyl dimethyl amine (SAPDMA)	0.50
Glyceryl monostearate	0.25
Citric acid	0.08
Sodium Citrate	0.05
Stearoxydimethicone	0.10
Silicone gum ¹	0.05
Cyclomethicone fluid	1.70
Spinosyn component	1.00
Water	q.s. to 100.00

¹ Silicone gum available from The General Electric Co. as SE-30 or SE-76 Gum.

This conditioner anti-lice product is made in a manner similar to that described in Example 7.

Example 9

Efficacy of Shampoo Formulations.

Shampoo formulations containing various concentrations of spinosad were used in this study. The formulations were prepared by wet milling for 30 minutes enough technical grade spinosad into a commercially available shampoo (Johnson's ® Baby Shampoo, Moisturizing Formula with Honey and Vitamin E, Johnson & Johnson Consumer Products, Inc.) to form a 10% stock spinosad/shampoo mixture. This mixture was diluted with additional shampoo to prepare the following spinosad concentrations: 10% (used

as originally prepared), 1%, 0.1% and 0.01% spinosad/shampoo (w/w).

5 The four concentrations of spinosad in shampoo and a control of tap water were tested against adult human body lice (*Pediculus humanus humanus*) according to a standard test, ASTM Standard E 938-83 (Reapproved 1988), that is available from the American Society for Testing and Materials, 100 Barr Harbor Drive, West Conshohocken, Pennsylvania USA [<http://www.astm.org/>]. In this test, 25 adult lice were immersed in each of the four shampoo concentrations for 10 minutes, then washed in water for 1 minute and rinsed in water for another minute. In the control group, 25 adult lice (*Pediculus humanus humanus*) were immersed in tap water for 10 minutes, then washed in water for 1 minute, and rinsed in water for another minute. A total of 5 trials were performed.

15 After one hour, the lice were examined to determine the knockdown number. "Knockdown" was measured as the rather quick (within a matter of one minute) immobilization of insect activity which leads from a moribund state to a state of kill. After 24 hours, the lice

were again examined to determine the number killed. The results of this study are summarized in Table 1.

5
XT 0580
Table 1: Comparison of Pediculicidal Effects of Spinosad in Shampoo at Various Concentrations

Mortality Data

Formulation	+1 hour % Knockdown	+24 hours % Mortality
Control	0.2	1.0
10% spinosad/shampoo	96.6	100.0
1% spinosad/shampoo	48.0	100.0
0.1% spinosad/shampoo	19.8	97.4
0.01% spinosad/shampoo	14.7	35.5

10
14
16
18
20
22
24
26
28
30
32
34
36
38
40
42
44
46
48
50
52
54
56
58
60
62
64
66
68
70
72
74
76
78
80
82
84
86
88
90
92
94
96
98
100
102
104
106
108
110
112
114
116
118
120
122
124
126
128
130
132
134
136
138
140
142
144
146
148
150
152
154
156
158
160
162
164
166
168
170
172
174
176
178
180
182
184
186
188
190
192
194
196
198
200
202
204
206
208
210
212
214
216
218
220
222
224
226
228
230
232
234
236
238
240
242
244
246
248
250
252
254
256
258
260
262
264
266
268
270
272
274
276
278
280
282
284
286
288
290
292
294
296
298
300
302
304
306
308
310
312
314
316
318
320
322
324
326
328
330
332
334
336
338
340
342
344
346
348
350
352
354
356
358
360
362
364
366
368
370
372
374
376
378
380
382
384
386
388
390
392
394
396
398
400
402
404
406
408
410
412
414
416
418
420
422
424
426
428
430
432
434
436
438
440
442
444
446
448
450
452
454
456
458
460
462
464
466
468
470
472
474
476
478
480
482
484
486
488
490
492
494
496
498
500
502
504
506
508
510
512
514
516
518
520
522
524
526
528
530
532
534
536
538
540
542
544
546
548
550
552
554
556
558
560
562
564
566
568
570
572
574
576
578
580
582
584
586
588
590
592
594
596
598
600
602
604
606
608
610
612
614
616
618
620
622
624
626
628
630
632
634
636
638
640
642
644
646
648
650
652
654
656
658
660
662
664
666
668
670
672
674
676
678
680
682
684
686
688
690
692
694
696
698
700
702
704
706
708
710
712
714
716
718
720
722
724
726
728
730
732
734
736
738
740
742
744
746
748
750
752
754
756
758
760
762
764
766
768
770
772
774
776
778
780
782
784
786
788
790
792
794
796
798
800
802
804
806
808
810
812
814
816
818
820
822
824
826
828
830
832
834
836
838
840
842
844
846
848
850
852
854
856
858
860
862
864
866
868
870
872
874
876
878
880
882
884
886
888
890
892
894
896
898
900
902
904
906
908
910
912
914
916
918
920
922
924
926
928
930
932
934
936
938
940
942
944
946
948
950
952
954
956
958
960
962
964
966
968
970
972
974
976
978
980
982
984
986
988
990
992
994
996
998
1000
1002
1004
1006
1008
1010
1012
1014
1016
1018
1020
1022
1024
1026
1028
1030
1032
1034
1036
1038
1040
1042
1044
1046
1048
1050
1052
1054
1056
1058
1060
1062
1064
1066
1068
1070
1072
1074
1076
1078
1080
1082
1084
1086
1088
1090
1092
1094
1096
1098
1100
1102
1104
1106
1108
1110
1112
1114
1116
1118
1120
1122
1124
1126
1128
1130
1132
1134
1136
1138
1140
1142
1144
1146
1148
1150
1152
1154
1156
1158
1160
1162
1164
1166
1168
1170
1172
1174
1176
1178
1180
1182
1184
1186
1188
1190
1192
1194
1196
1198
1200
1202
1204
1206
1208
1210
1212
1214
1216
1218
1220
1222
1224
1226
1228
1230
1232
1234
1236
1238
1240
1242
1244
1246
1248
1250
1252
1254
1256
1258
1260
1262
1264
1266
1268
1270
1272
1274
1276
1278
1280
1282
1284
1286
1288
1290
1292
1294
1296
1298
1300
1302
1304
1306
1308
1310
1312
1314
1316
1318
1320
1322
1324
1326
1328
1330
1332
1334
1336
1338
1340
1342
1344
1346
1348
1350
1352
1354
1356
1358
1360
1362
1364
1366
1368
1370
1372
1374
1376
1378
1380
1382
1384
1386
1388
1390
1392
1394
1396
1398
1400
1402
1404
1406
1408
1410
1412
1414
1416
1418
1420
1422
1424
1426
1428
1430
1432
1434
1436
1438
1440
1442
1444
1446
1448
1450
1452
1454
1456
1458
1460
1462
1464
1466
1468
1470
1472
1474
1476
1478
1480
1482
1484
1486
1488
1490
1492
1494
1496
1498
1500
1502
1504
1506
1508
1510
1512
1514
1516
1518
1520
1522
1524
1526
1528
1530
1532
1534
1536
1538
1540
1542
1544
1546
1548
1550
1552
1554
1556
1558
1560
1562
1564
1566
1568
1570
1572
1574
1576
1578
1580
1582
1584
1586
1588
1590
1592
1594
1596
1598
1600
1602
1604
1606
1608
1610
1612
1614
1616
1618
1620
1622
1624
1626
1628
1630
1632
1634
1636
1638
1640
1642
1644
1646
1648
1650
1652
1654
1656
1658
1660
1662
1664
1666
1668
1670
1672
1674
1676
1678
1680
1682
1684
1686
1688
1690
1692
1694
1696
1698
1700
1702
1704
1706
1708
1710
1712
1714
1716
1718
1720
1722
1724
1726
1728
1730
1732
1734
1736
1738
1740
1742
1744
1746
1748
1750
1752
1754
1756
1758
1760
1762
1764
1766
1768
1770
1772
1774
1776
1778
1780
1782
1784
1786
1788
1790
1792
1794
1796
1798
1800
1802
1804
1806
1808
1810
1812
1814
1816
1818
1820
1822
1824
1826
1828
1830
1832
1834
1836
1838
1840
1842
1844
1846
1848
1850
1852
1854
1856
1858
1860
1862
1864
1866
1868
1870
1872
1874
1876
1878
1880
1882
1884
1886
1888
1890
1892
1894
1896
1898
1900
1902
1904
1906
1908
1910
1912
1914
1916
1918
1920
1922
1924
1926
1928
1930
1932
1934
1936
1938
1940
1942
1944
1946
1948
1950
1952
1954
1956
1958
1960
1962
1964
1966
1968
1970
1972
1974
1976
1978
1980
1982
1984
1986
1988
1990
1992
1994
1996
1998
2000
2002
2004
2006
2008
2010
2012
2014
2016
2018
2020
2022
2024
2026
2028
2030
2032
2034
2036
2038
2040
2042
2044
2046
2048
2050
2052
2054
2056
2058
2060
2062
2064
2066
2068
2070
2072
2074
2076
2078
2080
2082
2084
2086
2088
2090
2092
2094
2096
2098
2100
2102
2104
2106
2108
2110
2112
2114
2116
2118
2120
2122
2124
2126
2128
2130
2132
2134
2136
2138
2140
2142
2144
2146
2148
2150
2152
2154
2156
2158
2160
2162
2164
2166
2168
2170
2172
2174
2176
2178
2180
2182
2184
2186
2188
2190
2192
2194
2196
2198
2200
2202
2204
2206
2208
2210
2212
2214
2216
2218
2220
2222
2224
2226
2228
2230
2232
2234
2236
2238
2240
2242
2244
2246
2248
2250
2252
2254
2256
2258
2260
2262
2264
2266
2268
2270
2272
2274
2276
2278
2280
2282
2284
2286
2288
2290
2292
2294
2296
2298
2300
2302
2304
2306
2308
2310
2312
2314
2316
2318
2320
2322
2324
2326
2328
2330
2332
2334
2336
2338
2340
2342
2344
2346
2348
2350
2352
2354
2356
2358
2360
2362
2364
2366
2368
2370
2372
2374
2376
2378
2380
2382
2384
2386
2388
2390
2392
2394
2396
2398
2400
2402
2404
2406
2408
2410
2412
2414
2416
2418
2420
2422
2424
2426
2428
2430
2432
2434
2436
2438
2440
2442
2444
2446
2448
2450
2452
2454
2456
2458
2460
2462
2464
2466
2468
2470
2472
2474
2476
2478
2480
2482
2484
2486
2488
2490
2492
2494
2496
2498
2500
2502
2504
2506
2508
2510
2512
2514
2516
2518
2520
2522
2524
2526
2528
2530
2532
2534
2536
2538
2540
2542
2544
2546
2548
2550
2552
2554
2556
2558
2560
2562
2564
2566
2568
2570
2572
2574
2576
2578
2580
2582
2584
2586
2588
2590
2592
2594
2596
2598
2600
2602
2604
2606
2608
2610
2612
2614
2616
2618
2620
2622
2624
2626
2628
2630
2632
2634
2636
2638
2640
2642
2644
2646
2648
2650
2652
2654
2656
2658
2660
2662
2664
2666
2668
2670
2672
2674
2676
2678
2680
2682
2684
2686
2688
2690
2692
2694
2696
2698
2700
2702
2704
2706
2708
2710
2712
2714
2716
2718
2720
2722
2724
2726
2728
2730
2732
2734
2736
2738
2740
2742
2744
2746
2748
2750
2752
2754
2756
2758
2760
2762
2764
2766
2768
2770
2772
2774
2776
2778
2780
2782
2784
2786
2788
2790
2792
2794
2796
2798
2800
2802
2804
2806
2808
2810
2812
2814
2816
2818
2820
2822
2824
2826
2828
2830
2832
2834
2836
2838
2840
2842
2844
2846
2848
2850
2852
2854
2856
2858
2860
2862
2864
2866
2868
2870
2872
2874
2876
2878
2880
2882
2884
2886
2888
2890
2892
2894
2896
2898
2900
2902
2904
2906
2908
2910
2912
2914
2916
2918
2920
2922
2924
2926
2928
2930
2932
2934
2936
2938
2940
2942
2944
2946
2948
2950
2952
2954
2956
2958
2960
2962
2964
2966
2968
2970
2972
2974
2976
2978
2980
2982
2984
2986
2988
2990
2992
2994
2996
2998
3000
3002
3004
3006
3008
3010
3012
3014
3016
3018
3020
3022
3024
3026
3028
3030
3032
3034
3036
3038
3040
3042
3044
3046
3048
3050
3052
3054
3056
3058
3060
3062
3064
3066
3068
3070
3072
3074
3076
3078
3080
3082
3084
3086
3088
3090
3092
3094
3096
3098
3100
3102
3104
3106
3108
3110
3112
3114
3116
3118
3120
3122
3124
3126
3128
3130
3132
3134
3136
3138
3140
3142
3144
3146
3148
3150
3152
3154
3156
3158
3160
3162
3164
3166
3168
3170
3172
3174
3176
3178
3180
3182
3184
3186
3188
3190
3192
3194
3196
3198
3200
3202
3204
3206
3208
3210
3212
3214
3216
3218
3220
3222
3224
3226
3228
3230
3232
3234
3236
3238
3240
3242
3244
3246
3248
3250
3252
3254
3256
3258
3260
3262
3264
3266
3268
3270
3272
3274
3276
3278
3280
3282
3284
3286
3288
3290
3292
3294
3296
3298
3300
3302
3304
3306
3308
3310
3312
3314
3316
3318
3320
3322
3324
3326
3328
3330
3332
3334
3336
3338
3340
3342
3344
3346
3348
3350
3352
3354
3356
3358
3360
3362
3364
3366
3368
3370
3372
3374
3376
3378
3380
3382
3384
3386
3388
3390
3392
3394
3396
3398
3400
3402
3404
3406
3408
3410
3412
3414
3416
3418
3420
3422
3424
3426
3428
3430
3432
3434
3436
3438
3440
3442
3444
3446
3448
3450
3452
3454
3456
3458
3460
3462
3464
3466
3468
3470
3472
3474
3476
3478
3480
3482
3484
3486
3488
3490
3492
3494
3496
3498
3500
3502
3504
3506
3508
3510
3512
3514
3516
3518
3520
3522
3524
3526
3528
3530
3532
3534
3536
3538
3540
3542
3544
3546
3548
3550
3552
3554
3556
3558
3560
3562
3564
3566
3568
3570
3572
3574
3576
3578
3580
3582
3584
3586
3588
3590
3592
3594
3596
3598
3600
3602
3604
3606
3608
3610
3612
3614
3616
3618
3620
3622
3624
3626
3628
3630
3632
3634
3636
3638
3640
3642
3644
3646
3648
3650
3652
3654
3656
3658
3660
3662
3664
3666
3668
3670
3672
3674
3676
3678
3680
3682
3684
3686
3688
3690
3692
3694
3696
3698
3700
3702
3704
3706
3708
3710
3712
3714
3716
3718
3720
3722
3724
3726
3728
3730
3732
3734
3736
3738
3740
3742
3744
3746
3748
3750
3752
3754
3756
3758
3760
3762
3764
3766
3768
3770
3772
3774
3776
3778
3780
3782
3784
3786
3788
3790
3792
3794
3796
3798
3800
3802
3804
3806
3808
3810
3812
3814
3816
3818
3820
3822
3824
3826
3828
3830
3832
3834
3836
3838
3840
3842
3844
3846
3848
3850
3852
3854
3856
3858
3860
3862
3864
3866
3868
3870
3872
3874
3876
3878
3880
3882
3884
3886
3888
3890
3892
3894
3896
3898
3900
3902
3904
3906
3908
3910
3912
3914
3916
3918
3920
3922
3924
3926
3928
3930
3932
3934
3936
3938
3940
3942
3944
3946
3948
3950
3952
3954
3956
3958
3960
3962
3964
3966
3968
3970
3972
3974
3976
3978
3980
3982
3984
3986
3988
3990
3992
3994
3996
3998
4000
4002
4004
4006
4008
4010
4012
4014
4016
4018
4020
4022
4024
4026
4028
4030
4032
4034
4036
4038
4040
4042
4044
4046
4048
4050
4052
4054
4056
4058
4060
4062
4064
4066
4068
4070
4072
4074
4076
4078
4080
4082
4084
4086
4088
4090
4092
4094
4096
4098
4100
4102
4104
4106
4108
4110
4112
4114
4116
4118
4120
4122
4124
4126
4128
4130
4132
4134
4136
4138
4140
4142
4144
4146
4148
4150
4152
4